REMARKS

In response to the Office action dated September 29, 2009, Applicants have amended claims 1 and 3 to promote clarity. Claims 1-7 are presented for examination.

Initially, Applicants would like to thank the Examiner and his supervisor for the telephone interview with their counsel held on January 26, 2010. An e-mail dated January 20, 2010 was sent to the Examiner to facilitate discussion in the interview. A copy of this e-mail is attached hereto as "Exhibit A" to serve as a partial summary of the interview. Other points discussed during the interview are summarized below.

Rejection under 35 U.S.C. §103(a)

The Office action rejects claims 1-7 as obvious on two grounds, each of which is traversed below:

I

Claims 1, 2, and 4-7 are rejected as obvious from Fuke et al., EP 0997182 ("Fuke") in view of Nakagawa et al., U.S. Patent No. 5,071,887 ("Nakagawa") and Kozawa et al., U.S. Patent No. 6,605,218 ("Kozawa").

Independent claim 1 is discussed first. Claim 1, as amended, covers bundles containing a plurality of selectively permeable polysulfone-based hollow fiber membranes, each of which has an inner surface for contacting blood and an outer surface for contacting a dialyzing fluid. The content of a hydrophilic polymer (e.g., polyvinyl pyrrolidone) in the outer surface of a hollow fiber membrane is 25 to 50 mass %. Further, the bundles of claim 1 exhibit, among others, two features: (1) any of extracted solutions from ten fractions of said bundle, obtained by dividing said bundle at substantially regular intervals along the lengthwise direction, shows a maximum value of smaller than 0.10 in UV absorbance at a wavelength of 220 to 350 nm, with the proviso that said extracted solutions are obtained by the extraction method for tests regulated in the approval manufacturing standards for dialytic artificial kidney devices; and (2) the difference between the maximum and the minimum out of the maximum values of UV absorbance of the extracted solutions from the respective fractions is not larger than 0.05.

Fuke describes a polysulfone type blood-purifying membrane that has improved blood compatibility and separation properties, and has less poly(vinylpyrrolidone) eluting in the

internal surface of the hollow fiber membrane. *See, e.g.*, the abstract. It states that polyvinyl pyrrolidone (PVP, a hydrophilic polymer) "is contained in the range of 1 to 10% by weight in the [entire] hollow fiber membrane." *See, e.g.*, the abstract and paragraphs [0011] and [0017], and claim 1. Further, Fuke states that

> "The important factor for the blood compatibility of the hollow fiber membranes is the hydrophilicity of the membrane surface which contacts blood, and in the PVP-containing polysulfone type hollow fiber membrane, the PVP concentration on the internal surface of the membrane is important. ... Accordingly, the surface PVP concentration in this invention is in the range of 30 to 45% [by weight], ..."

See paragraph [0023]; emphases added. It would have been apparent to one skilled in the art that Fuke describes using the internal surface of its hollow fiber membrane to contact blood and that the PVP content in the internal surface of its membrane is 30 to 45% by weight. Indeed, Fuke discusses the PVP content in the internal surface of its hollow fiber membrane in detail throughout paragraphs [0023]-[0025]. Thus, given that the PVP content in the entire membrane described in Fuke is at most 10% by weight and that the PVP content in the internal surface of the Fuke membrane is 30 to 45% by weight, one skilled in the art would readily recognize that the PVP content in the outer surface of Fuke's membrane is significantly lower than 10% by weight, let alone 25 to 50 mass % as recited by claim 1. In other words, Fuke does not disclose a membrane containing 25 to 50 mass % of a hydrophilic polymer in the outer surface, as recited by claim 1. Nor does Fuke render the membranes recited in claim 1 obvious. Indeed, Fuke emphasizes in paragraph [0023] the importance of maintaining high hydrophilicity of the membrane surface that contacts blood (i.e., the internal surface of the membrane) and therefore a high PVP concentration (i.e., 30 to 45% by weight) in that surface. In view of this teaching, one skilled in the art would not have modified Fuke's membrane by reducing the PVP concentration in the internal surface and increasing the PVP concentration in the outer surface to provide the membranes recited in claim 1.

The Office action asserts that "Fuke discloses a bundle of ... polysulfone-based hollow fiber membranes ... wherein the amount of hydrophilic polymer eluted is inhibited by cross-linking using radiation (paragraph 19, page 4), such that the amount of water-soluble PVP becomes 5 to 50% of the total amount." *See* page 3, last paragraph. It appears to be the Office

action's position that paragraph [0019] in Fuke discloses a membrane containing 5 to 50% PVP and therefore renders claim 1 obvious. The Office action clearly errs. Paragraph [0019] in Fuke merely states that the amount of water-soluble PVP (not the amount of all PVP) is 5 to 50% of the total amount of the PVP in the hollow fiber membrane (not the amount of membrane). In other words, the passage in paragraph [0019] quoted by the Office action is entirely irrelevant to determining the weight percentage of PVP in a membrane, let alone the weight percentage of PVP (i.e., 25-50 mass%) in the outer surface of a membrane as recited in claim 1. Note that Fuke repeatedly emphasizes that its membrane contains only 1 to 10% by weight of PVP. *See, e.g.*, the abstract, paragraph [0011] and [0017], and claim 1.

The Office action also asserts that "the concentration of PVP is determined from the total amount of PVP and polysulfone, based on this it is derivable that the concentration of PVP disclosed by Fuke is within the range claimed by applicant (see examples and above rejection)." *See* page 6, last paragraph; emphasis added. The Office action appears to assert that the Examples in Fuke disclose membranes containing 25 to 50% PVP in the outer surface as recited by claim 1. The Office action errs again. For example, Example 1 in Fuke discloses a polymer solution containing 17 parts by weight of a polysulfone and 7 parts by weight of PVP. In other words, the weight percentage of the PVP in the membrane produced by this polymer solution could be up to about 29% ($7 / (7+17) \approx 29\%$). However, Fuke explicitly teaches washing the membrane (e.g., by using hot water) to remove any excess PVP such that the amount of PVP is maintained at a level ranging from 1 to 10% of the total amount of the membrane. *See, e.g.*, paragraph [0052]. Indeed, Table 1 in Fuke lists the final compositions of the membranes described in the Examples. As shown in the second column in Table 1, the amounts of PVP in all Examples are below 9% of the total amount of the membrane, significantly less than 25 to 50% recited in claim 1. Note that the fourth column in Table 1 shows "surface PVP conc." It would have been apparent to one skilled in the art that these "surface PVP conc." refers to the PVP concentrations on the internal surface (which corresponds to the inner surface recited in claim 1), not the outer surface recited in claim 1. *See, e.g.*, Fuke, the abstract, paragraphs [0011] and [0023], and claim 1. In other words, one could readily recognize that the PVP content in the outer surface of Fuke's membrane is significantly lower than 10% by weight, let alone 25 to 50 mass % as recited by claim 1.

In sum, Fuke does not disclose or render obvious a membrane containing 25 to 50 mass % of a hydrophilic polymer in the outer surface, as recited by claim 1. Neither Nakagawa nor Kozawa cures the deficiencies in Fuke. Indeed, both references are entirely silent on a membrane containing 25 to 50 mass % of a hydrophilic polymer in the outer surface, as recited by claim 1.

In addition, none of Fuke, Nakagawa, and Kozawa discloses or renders obvious the two above-mentioned features recited in claim 1, i.e., (1) any of extracted solutions from ten fractions of said bundle, obtained by dividing said bundle at substantially regular intervals along the lengthwise direction, shows a maximum value of smaller than 0.10 in UV absorbance at a wavelength of 220 to 350 nm, with the proviso that said extracted solutions are obtained by the extraction method for tests regulated in the approval manufacturing standards for dialytic artificial kidney devices; and (2) the difference between the maximum and the minimum out of the maximum values of UV absorbance of the extracted solutions from the respective fractions is not larger than 0.05.

Thus, claim 1 would not have been obvious over Fuke in view of Nakagawa and Kozawa. As claims 2 and 4-7 depend from claim 1, they also would not have been obvious over Fuke in view of Nakagawa and Kozawa.

During the interview on January 26, 2010, the Examiner and his supervisor acknowledged that the obviousness rejection over Fuke, Nakagawa, and Kozawa is likely to be untenable, and indicated that they would reconsider the patentability of the claims in view of the other prior art known to them.

In addition, the Examiners appeared to indicate during the January 26, 2010 interview that they would not give patentable weight to the two above-mentioned features recited in claim 1. Applicants would like to remind the Examiners that, according to MPEP 2173.05(g),

> "A functional limitation is an attempt to define something by what it does, rather than by what it is (e.g., as evidenced by its specific structure or specific ingredients). There is nothing inherently wrong with defining some part of an invention in functional terms. …
>
> A functional limitation **must be** evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. … It was held that the

> limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. *In re Barr*, 444 F.2d 588, 170 USPQ 33 (CCPA 1971)" (emphasis added).

Here, claim 1 recites two functional limitations specified above. In other words, claim 1 covers bundles of membranes capable of performing the functions set forth by these two limitations and exclude those incapable of performing these functions. These two functional limitations set definite boundaries of the subject matter covered by claim 1 and therefore are perfectly acceptable. Accordingly, these two functional limitations **must be** evaluated when considering the patentability of claim 1.

II

Claim 3 is rejected as obvious from Fuke in view of Nakagawa and Van't Hoft et al., U.S. Patent No. 5,514,413 ("Van't Hoft").

Claim 3 incorporates the features of claim 1, which recites bundles containing a membrane having 25 to 50 mass % of a hydrophilic polymer in the outer surface and exhibiting the two above-mentioned features. As discussed above, neither Fuke nor Nakagawa discloses or renders obvious such a membrane.

Van't Hoft does not cure the deficiencies in Fuke and Nakagawa. Van't Hoft describes fabricating composite membranes by coating a porous substrate with a solution of selective polymer. *See, e.g.*, the abstract. However, Van't Hoft is entirely silent on a membrane having 25 to 50 mass % of a hydrophilic polymer in the outer surface, as well as the two above-mentioned features recited in claim 1.

Thus, claim 3 would not have been obvious from Fuke in view of Nakagawa and Van't Hoft.

In addition, claims 3 would not have been obvious from Fuke in view of Nakagawa and Van't Hoft on an additional, independent ground.

Claim 3 recites that the porosity of the outer surface of a hollow fiber membrane is 8 to 25%. The Office action asserts that "FUKE does not appear to explicitly disclose the specific range of the porosity on the outer surface. However, VAN'T HOFT discloses a surface porosity of 1 to 20% (Column 3, Lines 6-7)." *See* the paragraph bridging pages 5-6.

Applicants respectfully disagree. First, it would not have been obvious for one skilled in the art to combine Van't Hoft with Fuke to provide the membrane recited in claim 3. As discussed above, Fuke describes a polysulfone type blood-purifying membrane that has improved blood compatibility and separation properties. It is entirely silent on the porosity of the outer surface of its membrane. Fuke does not provide any teaching or suggestion that would have prompted one skilled in the art to modify its membrane to obtain 8 to 25% porosity in the outer surface, as recited in claim 3. Nor does the Office action provide any reason why one skilled in the art would have wanted to modify the membrane described in Fuke to obtain 8 to 25% porosity in the outer surface, as recited in claim 3.

As also discussed above, Van't Hoft describes a process of fabricating a composite membrane for gas separation. However, it does not disclose or suggest a membrane for dialysis described in Fuke, which is a field of use entirely different from that gas separation described in Van't Hoff. Thus, even if he or she had some reason to modify the membrane described in Fuke (which Applicants do not concede), one skilled in the art would not have looked to Van't Hoft for guidance. Further, Van't Hoft describes "fabricating composite membranes wherein a porous substrate, i.e., support membrane, is coated with a solution of permselective polymer formulated in a solvent medium, which, under normal conditions, dissolves, partially dissolves, or adversely interacts with the substrate material." *See* column 2, lines 35-40. It also describes that such composite membranes "are fabricated by forming a porous substrate membrane and incorporating a reserve of a non-solvent medium in the substrate membrane pore network and applying the coating solution onto the wetted substrate surface." *See* column 2, lines 44-48. The manufacturing process described in Van't Hoft is entirely different from the processes described in Fuke, which produces a membrane by either (1) subjecting a polymer solution to extrusion and spinning or (2) spinning a hollow fiber membrane using a polymer solution and then insolubilizing a portion of poly(vinylpyrrolidone) in the hollow fiber membrane (*see* paragraphs [0012] and [0013]). Thus, given the significant differences between the process described in Van't Hoft and those described in Fuke, one skilled in the art would not have looked to Van't Hoft for guidance when considering modifying the membrane described in Fuke. Indeed, according to Fuke,

> "[t]he present inventors have diligently made an examination for achieving the above-mentioned purposes and have consequently found that a clean, hollow fiber membrane which is low in the amount of polyvinyl pyrrolidone ... eluted from the internal surface ... can be provided by water-insolubilizing a portion of the PVP of a PVP-containing polysulfone type hollow fiber membrane to an appropriate value ... by extracting the PVP with an adequate solvent, ..."

See paragraph [0010]. Thus, it would have been apparent to one skilled in the art that replacing the processes described in Fuke with that described in Van't Hoft (which does not involve a water-insolubilizng step) to achieve a porosity of 8 to 25% in the outer surface of a membrane would not reduce the amount of the eluted poly(vinylpyrrole) and would therefore defeat the intended purpose of the membrane described in Fuke. As explained in the MPEP 2143.01V, "The proposed modification cannot render the prior art unsatisfactory for its intended purpose. If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification."

Further, even if Van't Hoft were somehow combined with Fuke and Nakagawa, the combination would still not have been the membrane recited in claim 3. Specifically, Fuke, Van't Hoft, and Nakagawa all fail to recognize the criticality of a porosity of 8% to 25% in the outer surface of a membrane. According to the specification,

> "the porosity of the outer surface of the hollow fiber membrane is preferably 8 to 25%, ... in order to impart the above described characteristics to the membrane. When the porosity and average pore area are too small [e.g., smaller than 8%], ... the module-fabricating workability tends to lower, since the hollow fiber membranes are stuck to one another because of the hydrophilic polymer on the outer surfaces of the membranes, while the membranes are being dried. .... when the porosity and the average pore area are too large [e.g., higher than 25%], the percentage of void of the hollow fiber membrane becomes too high, and the burst pressure tends to lower."

See paragraph [0082]. In other words, the specification teaches that a porosity of 8% to 25% is critical in achieving a suitable module-fabricating workability while still maintaining a proper burst pressure for the hollow fiber membranes. By contrast, none of Fuke, Van't Hoft, and Nakagawa recognizes this criticality. Indeed, as discussed above, Fuke focuses on the PVP content in the internal surface, not the outer surface, of its membrane. Thus, even if Fuke, Van't Hoft, and Nakagawa were somehow combined, one skilled in the art would at most modify the

porosity of the internal surface of Fuke's membrane, but would not have been prompted to modify the outer surface of Fuke's membrane, let alone modifying the porosity of the outer surface of Fuke's membrane to 8% to 25%, as recited in claim 3.

For the reasons set forth above, claim 3 would not have been obvious from Fuke in view of Nakagawa and Van't Hoft on this additional, independent ground.

Double patenting rejections

Claims 1-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over (1) claims 1-9 of co-pending Application No. 10/559,544 and (2) claims 1-6, 16, and 17 of co-pending Application No. 10/599,167.[1] Applicants request that these two rejections be held in abeyance until claims 1-7 are otherwise in condition for allowance.

CONCLUSION

Applicants submit that the obviousness rejections asserted by the final Office action have been overcome.

Any circumstance in which Applicants have: (a) addressed certain comments of the Examiner does not mean that Applicants concede other comments of the Examiner; and (b) made arguments for the patentability of some claims does not mean that there are not other good reasons for the patentability of those claims and other claims.

[1] Applicants note that U.S. Application No. 10/559,544 was issued as U.S. Patent No.7,638,052 on December 29, 2009.

Please apply any other charges to deposit account 06-1050, referencing Attorney's Docket No. 19461-0004US1.

Respectfully submitted,

Date: January 28, 2010

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EXHIBIT A

Tony Zhang

From: Tony Zhang
Sent: Wednesday, January 20, 2010 5:50 PM
To: 'Dirk.Bass@uspto.gov'
Cc: Samuel Borodach
Subject: U.S. Application No. 10/582,052 (Our Ref.:19461-0004US1)

Dear Examiner Bass,

Thank you for discussing with me the non-final office action issued on September 29, 2009 in this patent application.

You asked me to send you an outline of any arguments in addition to those previously presented so that you could evaluate whether we should have another telephone interview. I provide the outline below, which is focused on the obviousness rejection of claim 1 over Fuke in view of Nakagawa and Kozawa.

By way of background, we conducted a telephone interview with Examiner Christian on August 21, 2009 to discuss the patentability of the claims. During the interview, we pointed out that Fuke, the primary reference, describes using the internal surface of its hollow fiber membrane to contact blood and that the PVP content in the internal surface of its membrane is 30 to 45% by weight. *See, e.g.,* Fuke, paragraphs [0011] and [0023], and claim 1. Thus, given that the PVP content in the entire membrane described in Fuke is at most 10% by weight (*see, e.g.*, Fuke, paragraphs [0011] and [0023], and claim 1), one skilled in the art would readily recognize that the PVP content in the outer surface of Fuke's membrane is significantly lower than 10% by weight, let alone 25 to 50 mass % as recited by claim 1.

Examiner Christian pointed out during the interview that it is not entirely clear whether the phrase "outer surface" recited in claim 1 includes the internal surface that contacts blood. To promote clarity, we proposed to amend claim 1 to recite "each hollow fiber membrane has an inner surface for contacting blood and an outer surface for contacting a dialyzing fluid." At the end of the interview, Examiner Christian indicated that she believes that this amendment should overcome the obviousness rejection over Fuke in view of Nakagawa and Kozawa, but asked us to file a response including our proposed amendment to claim 1 so that she can reconsider the patentability of this claim in view of other prior art known to her. We filed the response as suggested by Examiner Christian on September 9, 2009.

However, in the office action issued on September 29, 2009, Examiner Christian maintained the previous obviousness rejection of claim 1 citing the same three references. It appears that Examiner Christian now relies on different sections in Fuke to support her obviousness rejection. We address the two most relevant assertions made by Examiner Christian below.

First, Examiner Christian asserts that "Fuke discloses a bundle of ... polysulfone-based hollow fiber membranes ... wherein the amount of hydrophilic polymer eluted is inhibited by cross-linking using radiation (paragraph 19, page 4), such that the amount of water-soluble PVP becomes 5 to 50% of the total amount." *See* page 3, last paragraph of the office action. It appears to be Examiner Christian's position that paragraph [0019] in Fuke discloses a membrane containing 5 to 50% PVP and therefore renders claim 1 obvious. Examiner

Christian clearly errs. Paragraph [0019] in Fuke merely states that the amount of water-soluble PVP (not the amount of all PVP) is 5 to 50% of the total amount of the PVP in the hollow fiber membrane (not the amount of membrane). In other words, the passage in paragraph [0019] quoted by Examiner Christian is entirely irrelevant to the weight percentage of PVP in a membrane, let alone the weight percentage of PVP (i.e., 25-50 mass%) in the outer surface of the membrane as recited in claim 1. Note that Fuke repeatedly emphasizes that its membrane contains 1 to 10% by weight of PVP. *See, e.g.*, the abstract, paragraph [0011] and [0017], and claim 1.

Second, Examiner Christian asserts that our previous arguments are not persuasive because "the concentration of PVP is determined from the total amount of PVP and polysulfone, based on this it is derivable that the concentration of PVP disclosed by Fuke is within the range claimed by applicant (see examples and above rejection)." *See* page 6, last paragraph of the office action; emphasis added. Examiner Christian appears to assert that the Examples in Fuke disclose membranes containing 25 to 50% PVP in the outer surface as recited by claim 1. Examiner Christian errs again. For example, Example 1 in Fuke discloses a polymer solution containing 17 parts by weight of a polysulfone and 7 parts by weight of PVP. In other words, the weight percentage of the PVP in the membrane produced by this polymer solution could be up to about 29% (7 / (7+17) ≈ 29%). However, Fuke explicitly teaches washing the membrane (e.g., by using hot water) to remove any excess PVP such that the amount of PVP is maintained at a level ranging from 1 to 10% of the total amount of the membrane. *See, e.g.*, paragraph 52. Indeed, Table 1 in Fuke lists the final compositions of the membranes described in the Examples. As shown in the second column in Table 1, the amounts of PVP in all Examples are below 9% of the total amount of the membrane, significantly less than 25 to 50% recited by claim 1. Note that the fourth column in Table 1 shows "surface PVP conc." It would have been apparent to one skilled in the art that these "surface PVP conc." refers to the PVP concentrations on the internal surface (which corresponds to the inner surface recited in claim 1), not the outer surface recited in claim 1. *See, e.g.*, Fuke, the abstract, paragraphs [0011] and [0023], and claim 1. In other words, one could readily recognize that the PVP content in the outer surface of Fuke's membrane is significantly lower than 10% by weight, let alone 25 to 50 mass % as recited by claim 1.

Neither of the other two secondary references cited in the office action discloses the amount of PVP in the outer surface of a hollow fiber membrane and therefore does not cure the deficiencies in Fuke.

For at least the reasons set forth above, we believe that the obviousness rejection of claim 1 in the office action should be withdrawn. If you have any question, we would be happy to discuss the patentability of claim 1 in a telephone interview.

Incidentally, the Applicant would like to work with you to move this application toward allowance as soon as possible. Thus, if you feel that the arguments above are not sufficient to overcome the obviousness rejection of claim 1, we ask you to kindly provide us with suggestions what additional amendment is needed to place claim 1 in condition for allowance.

As the next deadline for filing a response to the office action is January 29, 2010, we look forward to prompt reply so that we can file the response by that deadline.

Regards,
Tony

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